

**Renal Cell Carcinoma Staging
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. <i>CA Cancer J Clin</i> 2007; 57(1):43-66.	15	N/A	Report and examine data on cancer incidence death, and survival.	N/A	N/A
2. Leslie JA, Prihoda T, Thompson IM. Serendipitous renal cell carcinoma in the post-CT era: continued evidence in improved outcomes. <i>Urol Oncol</i> 2003; 21(1):39-44.	13	257	To compare patient and tumor characteristics between serendipitous and non-serendipitously discovered renal cell carcinoma (RCC) in the recent widespread use of CT and US. Tumor registry was reviewed for diagnosis and treatment of RCC.	Use of CT and US has led to the discovery of many asymptomatic lesions, including renal tumors.	2
3. Lightfoot N, Conlon M, Kreiger N, et al. Impact of noninvasive imaging on increased incidental detection of renal cell carcinoma. <i>Eur Urol</i> 2000; 37(5):521-527.	13	172	To determine effect of CT and US on the incidental detection of RCC.	Incidentally detected tumors now constitute the majority of cancers detected in some series. Either US or CT imaging detected over 80% of the incidentally detected tumors.	2
4. Stenzl A, deKernion JB. The natural history of renal cell carcinoma. <i>Semin Urol</i> 1989; 7(3):144-148.	12	N/A	To review history of RCC.	No results stated.	4
5. Flanigan RC, Campbell SC, Clark JI, Picken MM. Metastatic renal cell carcinoma. <i>Curr Treat Options Oncol</i> 2003; 4(5):385-390.	12	N/A	To review management of patients with metastatic RCC.	Metastases may be found at diagnosis or at some interval after nephrectomy. A shorter interval between nephrectomy and the development of metastases is linked with poorer prognosis. Patients with metastatic RCC face a dismal prognosis, with a median survival time of only 6 to 12 months and a 2-year survival rate of 10% to 20%.	3
6. Guinan PD, Vogelzang NJ, Fremgen AM, et al. Renal cell carcinoma: tumor size, stage and survival. Members of the Cancer Incidence and End Results Committee. <i>J Urol</i> 1995; 153(3 Pt 2):901-903.	13	2473	Review records of patients with histological diagnosis of RCC to define the relationship among tumor size, stage and survival.	Tumor size was related to stage and survival. Larger tumors were generally associated with an increased stage ($P \leq 0.0005$) and poorer survival ($P \leq 0.005$).	2
7. Frank I, Blute ML, Leibovich BC, Chevillet JC, Lohse CM, Zincke H. Independent validation of the 2002 American Joint Committee on cancer primary tumor classification for renal cell carcinoma using a large, single institution cohort. <i>J Urol</i> 2005; 173(6):1889-1892.	15	2,746	To evaluate the 2002 primary tumor classification and compare its predictive ability with that of the 1997 classification.	2002 primary tumor classification with pT1 cancers sub-classified into pT1a and pT1b provides excellent stratification of patients according to cancer specific survival and it has a predictive ability that is superior to that of the 1997 classification.	2
8. Gattman MT, Blute ML. Update on pathologic staging of renal cell carcinoma. <i>Urology</i> 2002; 60(2):209-217.	13	N/A	Review of the prognostic significance of the revised 1997 TNM staging.	The 1997 TNM system is a significant predictor of prognosis when comparing stage I and stage IV although staging between pT2 and pT3 classifications show little survival differences.	2

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9. Greene FL, Page DL, Fleming ID, et al. Kidney. <i>American Joint Committee on Cancer. AJCC Cancer Staging Manual</i> . 6th ed. New York, NY: Springer-Verlag; 2002:355-360.	15	N/A	Cancer staging manual.	N/A	NA
10. Yoon J, Herts BR. Staging renal cell carcinoma with helical CT: the revised 1997 AJCC and UICC TNM criteria. <i>Crit Rev Comput Tomogr</i> 2003; 44(4):229-249.	12	N/A	Review state of the art helical CT in RCC staging with discussion of 1997 revised TNM staging.	CT of the kidneys plays a key role in the detection, characterization, and staging of RCC, and for surgical planning.	3
11. Tsui KH, Shvarts O, Smith RB, Figlin RA, deKernion JB, Belldegrun A. Prognostic indicators for renal cell carcinoma: a multivariate analysis of 643 patients using the revised 1997 TNM staging criteria. <i>J Urol</i> 2000; 163(4):1090-1095; quiz 1295.	13	643	Retrospective review to determine independent prognostic indicators for RCC using the revised 1997 TNM staging criteria.	T3 and T4 renal cell tumor staging predicts decreased survival; TNM stage and grade of disease were the most important prognostic indicators.	2
12. Frank W, Guinan P, Stuhldreher D, Saffrin R, Ray P, Rubenstein M. Renal cell carcinoma: the size variable. <i>J Surg Oncol</i> 1993; 54(3):163-166.	3c	337	To compare 5 year survival with size of tumor at diagnosis.	Inverse correlation between tumor size and survival.	2
13. Hsu RM, Chan DY, Siegelman SS. Small renal cell carcinomas: correlation of size with tumor stage, nuclear grade, and histologic subtype. <i>AJR</i> 2004; 182(3):551-557.	3c	213	Retrospective review to correlate size of RCC with tumor stage, nuclear grade, and histologic subtype in patients treated using partial or radical nephrectomy.	Of 50 lesions ≤ 3 cm 38% were T3a, and 28% were high grade (Fuhrman 3, 4). Lesions < 5 cm had the same T-stage.	2
14. Catalano C, Fraioli F, Laghi A, et al. High-resolution multidetector CT in the preoperative evaluation of patients with renal cell carcinoma. <i>AJR</i> 2003; 180(5):1271-1277.	10	40	To determine the accuracy of multidetector CT (MDCT) using a high resolution technique in preoperative evaluation of patients with RCC.	For Robson stage I of RCC, fat infiltration on 1 mm scans was diagnosed with 96% sensitivity, 93% specificity, and 95% accuracy; PPV of 100% , NPV of 93%. MDCT is an accurate technique.	2
15. Hallscheidt PJ, Bock M, Riedasch G, et al. Diagnostic accuracy of staging renal cell carcinomas using multidetector-row computed tomography and magnetic resonance imaging: a prospective study with histopathologic correlation. <i>J Comput Assist Tomogr</i> 2004; 28(3):333-339.	9	82	Prospective study to compare accuracy of MDCT and MRI in staging RCC.	MRI achieved accuracy of 78%-87% and CT 80%-83%, which are statistically identical. MRI and CT can be used interchangeably for staging renal cancer.	2

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16. Walter C, Kruessell M, Gindele A, Brochhagen HG, Gossmann A, Landwehr P. Imaging of renal lesions: evaluation of fast MRI and helical CT. <i>Br J Radiol</i> 2003; 76(910):696-703.	9	29	To compare triphasic helical CT and fast MRI for staging renal cancer.	12 of 18 renal cancers were correctly staged by CT and MRI. Both MRI and CT are excellent in providing critical staging information, however, CT does so more quickly.	2
17. Roberts WW, Bhayani SB, Allaf ME, Chan TY, Kavoussi LR, Jarrett TW. Pathological stage does not alter the prognosis for renal lesions determined to be stage T1 by computerized tomography. <i>J Urol</i> 2005; 173(3):713-715.	13	186	Retrospective review to determine if radiographically staged clinical T1 lesions that were pathological T1 behave differently than those that were clinical stage T1 and up staged to pT3a.	5-year recurrence free survival was not statistically different in patients with pT1 and pT3a lesions (90.6% and 97.5%, respectively). Smaller tumors (<7 cm) upgraded to T3b based on capsule invasion behave like T1 tumors and exact pathologic T staging does not appear to impact overall survival.	2
18. Kamel IR, Hochman MG, Keogan MT, et al. Accuracy of breath-hold magnetic resonance imaging in preoperative staging of organ-confined renal cell carcinoma. <i>J Comput Assist Tomogr</i> 2004; 28(3):327-332.	10	43	Retrospective study to determine accuracy of breath-hold MRI for preoperative staging of organ-confined (stage I) RCC.	MRI has accuracy of range 80% and 82% in staging patients with organ-confined RCC, with 90% agreement between readers.	2
19. Roy C, Sr., El Ghali S, Buy X, et al. Significance of the pseudocapsule on MRI of renal neoplasms and its potential application for local staging: a retrospective study. <i>AJR</i> 2005; 184(1):113-120.	10	80 tumors	Retrospective study to evaluate the role of MRI in showing a tumoral pseudocapsule to select patients for partial surgery.	<ul style="list-style-type: none"> • MRI findings for isolated analysis of the pseudocapsule for differentiating stage T1/T2 from T3a were sensitivity: 86%, 50%; specificity: 95%, 92%; PPV: 95%, 33%; NPV: 88%, 92%; and accuracy: 93%, 89%, for clear cell and papillary types, respectively. • For stage T3a, with both abnormalities of the pseudocapsule and perirenal fat, results were, for overall RCC sensitivity: 84%; specificity: 95%; PPV: 91%; NPV: 91%; and accuracy: 91%. • The presence of an intact pseudocapsule is a sign of lack of perinephric fat invasion and predicts that the tumor can be removed by nephron-sparing surgery. 	2
20. Sawai Y, Kinouchi T, Mano M, et al. Ipsilateral adrenal involvement from renal cell carcinoma: retrospective study of the predictive value of computed tomography. <i>Urology</i> 2002; 59(1):28-31.	10	73	Retrospective analysis to assess the value of CT in detecting ipsilateral adrenal involvement by RCC.	CT had 100% sensitivity, 76% specificity, 11% PPV, and 100% NPV for ipsilateral adrenal involvement of RCC. Normal adrenal images on CT could exclude adrenal involvement by RCC, but radical nephrectomy should be performed in patients with large tumors.	2

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21. Hatcher PA, Paulson DF, Anderson EE. Accuracy in staging of renal cell carcinoma involving vena cava. <i>Urology</i> 1992; 39(1):27-30.	13	44	To examine pathologic up-staging or down-staging of RCC and its impact on patient selection for surgery.	Radiographic staging of extracapsular tumor extension and regional lymphadenopathy is unreliable, but current radiographic techniques delineate the level of thrombus extension for surgical approach with high accuracy.	3
22. Miles KA, London NJ, Lavelle JM, Messios N, Smart JG. CT staging of renal carcinoma: a prospective comparison of three dynamic computed tomography techniques. <i>Eur J Radiol</i> 1991; 13(1):37-42.	9	70	To prospectively compare and describe three CT methods used for staging RCC.	<ul style="list-style-type: none"> • Techniques using single location scanning were more accurate in demonstrating tumor involvement of the renal vein and inferior vena cava (IVC) but were less accurate in assessing extracapsular spread. • Technique 3 (single location sequence at the level of the renal veins and a rapid bolus incremental dynamic technique) was the most accurate in the diagnosis of lymph-node involvement. 	2
23. Hallscheidt PJ, Fink C, Haferkamp A, et al. Preoperative staging of renal cell carcinoma with inferior vena cava thrombus using multidetector CT and MRI: prospective study with histopathological correlation. <i>J Comput Assist Tomogr</i> 2005; 29(1):64-68.	9	23	Prospective study to evaluate the accuracy of MDCT and MRI in staging RCC with caval thrombus.	<ul style="list-style-type: none"> • CT thrombus detection sensitivity and specificity for both readers was 0.93 and 0.8 respectively. • MRI sensitivity and specificity for both readers was 1.0/0.85 and 0.75. • CT and MR accuracy was 78% and 72%, 88% and 76% respectively. 	2
24. Laissy JP, Menegazzo D, Debray MP, et al. Renal carcinoma: diagnosis of venous invasion with Gd-enhanced MR venography. <i>Eur Radiol</i> 2000; 10(7):1138-1143.	10	36	Prospective, blinded study to evaluate the value of gadolinium-enhanced time-of-flight MR venography (MRV) in the diagnosis of bland thrombosis/tumoral invasion in the preoperative assessment of RCC. Preoperative precontrast and enhanced GRE fast low angle shot (FLASH) images were compared with pre- and post-contrast T1-weighted images.	Precontrast spin-echo (SE) and FLASH images were 88% sensitive and 100% specific respectively, and enhanced FLASH images were 100% sensitive and 96% specific. The nature of thrombus (neoplastic or bland) was more accurately assessed (McNemar's, $p < 0.05$) with FLASH-enhanced MRI (sensitivity 89%; specificity 96%) than with SE and pre-contrast FLASH images (sensitivity 79%; specificity 94%). Gd-enhanced MRV might improve preoperative assessment of vascular involvement in renal carcinoma.	2

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25. Ergen FB, Hussain HK, Caoili EM, et al. MRI for preoperative staging of renal cell carcinoma using the 1997 TNM classification: comparison with surgical and pathologic staging. <i>AJR</i> 2004; 182(1):217-225.	10	40	Retrospective review to determine accuracy of MRI for preoperative staging of RCC using the 1997 TNM classification.	Agreement between MRI and surgical-pathologic staging was good for T staging (kappa = 0.72 and 0.78 for reviewers 1 and 2 respectively), poor for N staging (kappa = 0.13, both reviewers), good for M staging (kappa = 0.66, both reviewers), and excellent for the assessment of venous involvement (kappa = 0.93, both reviewers). MRI is reliable, in particular assessing venous involvement.	3
26. Bos SD, Mensink HJ. Can duplex Doppler ultrasound replace computerized tomography in staging patients with renal cell carcinoma? <i>Scand J Urol Nephrol</i> 1998; 32(2):87-91.	9	66	To compare the accuracy and reliability of duplex Doppler US and CT in staging patients with RCC.	T stage determined correctly by US in 56 and by CT in 50; of 14 with vascular tumor thrombi 13 were correctly identified by US, 12 by CT. Doppler US highly accurate in diagnosis and extent of thrombus.	2
27. Horan JJ, Robertson CN, Choyke PL, et al. The detection of renal carcinoma extension into the renal vein and inferior vena cava: a prospective comparison of venacavography and magnetic resonance imaging. <i>J Urol</i> 1989; 142(4):943-947; discussion 947-948.	9	44	Prospective comparison of venacavography and MRI for staging RCC.	<ul style="list-style-type: none"> • Venacavography and MRI correctly identified 9 of the 11 patients (82%) with IVC thrombus. • Venacavography was slightly more sensitive (71%) in identifying the presence of renal vein thrombus than MRI (65%). MRI localized the thrombus within the renal vein better. • Venacavography and MRI offer equal diagnostic accuracy in the identification of venous extension of RCC. The combination of both tests results in higher diagnostic yield than either test alone. Neither test by itself is reliable in the presence of a large, bulky adenopathic lesion. 	2
28. London NJ, Messios N, Kinder RB, et al. A prospective study of the value of conventional CT, dynamic CT, ultrasonography and arteriography for staging renal carcinoma. <i>Br J Urol</i> 1989; 64(3):209-217.	9	28	Prospective comparison of the value of dynamic CT, conventional CT, US and arteriography in staging RCC.	<ul style="list-style-type: none"> • Arteriography correctly staged 48% of tumors. • US and conventional CT correctly staged 50%. • Dynamic CT correctly staged 72%. • Dynamic CT staged more accurately than US, conventional CT or arteriography. 	2
29. Krestin GP, Gross-Fengels W, Marincek B. [The importance of magnetic resonance tomography in the diagnosis and staging of renal cell carcinoma]. <i>Radiologe</i> 1992; 32(3):121-126.	9	79	To determine the value of MRI in the diagnosis and staging of RCC by comparing MRI with CT and histologic staging.	T-stage was predicted correctly with CT in 78.4% and with MRI in 84.0% of the cases, while the N-stage was accurately assessed in 81.8% and 79.5%, respectively. MRI is a true alternative to CT.	2

* See Last Page for Key

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30. Nishimura K, Hida S, Okada K, Yoshida O, Nishimura K. Staging and differential diagnosis of renal cell carcinoma: a comparison of magnetic resonance imaging (MRI) and computed tomography (CT). <i>Hinyokika Kyo</i> 1988; 34(8):1323-1331.	9	29	To compare the value of CT with MRI in staging of RCC.	MRI and CT showed similar results, but MRI may be more sensitive in detecting the venous extension, metastatic adenopathy, and adjacent organ invasion. The percent contrast value of the T1 weighted images was 50% or less in 3 patients, and that of the T2 weighted images was 50% or more in 2 patients and 21%-38% in the others.	3
31. Guimaraes AR, Tabatabei S, Dahl D, McDougal WS, Weissleder R, Harisinghani MG. Pilot study evaluating use of lymphotropic nanoparticle-enhanced magnetic resonance imaging for assessing lymph nodes in renal cell cancer. <i>Urology</i> 2008; 71(4):708-712.	14	9	To assess lymphotropic nanoparticle-enhanced MRI in identifying malignant nodal involvement in patients with renal neoplasms.	Lymphotropic nanoparticle-enhanced MRI had high sensitivity (100%) and specificity (95.7%) in renal neoplasms.	4
32. Fritzsche PJ, Millar C. Multimodality approach to staging renal cell carcinoma. <i>Urol Radiol</i> 1992; 14(1):3-7.	12	N/A	To compare advantages and limitations of US, CT, MRI in staging RCC.	US and MRI are good for patients with compromised renal function preventing administration of iodinated contrast material or those who have experienced reactions to contrast.	4
33. Kabala JE, Gillatt DA, Persad RA, Penry JB, Gingell JC, Chadwick D. Magnetic resonance imaging in the staging of renal cell carcinoma. <i>Br J Radiol</i> 1991; 64(764):683-689.	9	24	Prospective study to compare CT and MRI in staging of RCC.	IVC was well demonstrated with MRI in all cases. In 14 out of 15, MRI and operative staging were in agreement. MRI and CT staging were in agreement in 16 out of the 17 patients where both were performed.	3
34. Lim DJ, Carter MF. Computerized tomography in the preoperative staging for pulmonary metastases in patients with renal cell carcinoma. <i>J Urol</i> 1993; 150(4):1112-1114.	9	120	To evaluate the role of CT in examining the chest for staging RCC. Patients had chest radiography and chest CT.	Results of chest radiography and chest CT were normal in 82 and abnormal in 23. In patients with a relatively small tumor (stage T1) a normal chest radiograph is adequate for pulmonary staging.	2
35. Fielding JR, Aliabadi N, Renshaw AA, Silverman SG. Staging of 119 patients with renal cell carcinoma: the yield and cost-effectiveness of pelvic CT. <i>AJR</i> 1999; 172(1):23-25.	13	119	Computerized review of medical records to determine the yield and cost-effectiveness of pelvic CT in staging RCC.	CT has insignificant yield and should not be routinely performed. The findings on CT of the pelvis did not generate a significant number of other tests.	2
36. Benson MA, Haaga JR, Resnick MI. Staging renal carcinoma. What is sufficient? <i>Arch Surg</i> 1989; 124(1):71-73.	9	64	Retrospective review of patients with RCC to assess roles of angiography, venography, bone scan, US, CT and MRI.	CT is useful for overall staging. Venacavography is not indicated if CT has excluded caval thrombus. Routine bone scans are not necessary in the absence of an elevated alkaline phosphatase level or bone pain.	3

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37. Campbell RJ, Broaddus SB, Leadbetter GW, Jr. Staging of renal cell carcinoma: cost-effectiveness of routine preoperative bone scans. <i>Urology</i> 1985; 25(3):326-329.	15	42	Retrospective analysis of the cost-effectiveness of routine preoperative bone scans in patients with RCC.	Bone scans are not cost-effective as a routine preoperative tool because they do not alter outcome.	3
38. Marshall ME, Pearson T, Simpson W, Butler K, McRoberts W. Low incidence of asymptomatic brain metastases in patients with renal cell carcinoma. <i>Urology</i> 1990; 36(4):300-302.	10	106	To determine the value of routine CT scanning of the brain in patients with RCC.	78.6% of patients with brain metastases had central nervous system symptoms; only 3.3% of patients without symptoms had metastases. CT of brain should only be done for symptomatic patients.	2
39. Kang DE, White RL, Jr., Zuger JH, Sasser HC, Teigland CM. Clinical use of fluorodeoxyglucose F 18 positron emission tomography for detection of renal cell carcinoma. <i>J Urol</i> 2004; 171(5):1806-1809.	9	66	Retrospective review to evaluate role of FDG-PET in patients with RCC. Accuracies of PET, chest CT, abdominal/pelvic CT and bone scan were compared.	<ul style="list-style-type: none"> • For primary tumors, PET had sensitivity of 60% and specificity of 100%, CT had sensitivity of 91.7% and specificity of 100%. • For lymph node metastases PET had sensitivity of 75% and specificity of 100%. CT had sensitivity of 92.6% and specificity of 98.1%. • For metastases to the lung parenchyma, PET had sensitivity of 75% and specificity of 97% compared to 91.1% and 73.1%, respectively, for chest CT. • For bone metastases, PET had sensitivity of 77.3% and specificity of 100.0%, compared to 93.8% and 87.2% for combined CT and bone scan. • PET may have a complementary role as a problem solving tool in cases that are equivocal. 	2
40. Majhail NS, Urbain JL, Albani JM, et al. F-18 fluorodeoxyglucose positron emission tomography in the evaluation of distant metastases from renal cell carcinoma. <i>J Clin Oncol</i> 2003; 21(21):3995-4000.	10	24	To evaluate role of FDG-PET in detection of distant metastases from RCC.	FDG-PET had sensitivity of 63.6%, specificity of 100%, PPV of 100%. FDG-PET may not characterize small lesions; may complement anatomic studies and decide need for biopsy in some cases. Negative PET does not exclude active malignancy.	2
41. Choyke PL, Walther MM, Wagner JR, Rayford W, Lyne JC, Linehan WM. Renal cancer: preoperative evaluation with dual-phase three-dimensional MR angiography. <i>Radiology</i> 1997; 205(3):767-771.	4	18	To evaluate use of dual-phase 3D MRA in the preoperative staging of renal cancer. Imaging results were compared with surgical findings.	30 of 31 renal arteries were detected with MRA. MRA with dual phase technique also detected the venous thrombi, venous collaterals and depicted the relationship between nodes and renal arteries.	3
42. Hilton S. Imaging of renal cell carcinoma. <i>Semin Oncol</i> 2000; 27(2):150-159.	12	N/A	To review current imaging methods in RCC.	There is an expanding role for minimally invasive surgery which requires more accurate depiction of vessels and nodal staging.	4

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43. Miller K. Renal cell carcinoma. Guidelines for diagnosis and treatment. <i>Urol Int</i> 1999; 63(1):6-9.	12	N/A	To review current diagnostic and treatment methods in RCC.	Increasing use of imaging and demand for accurate assessment of imaging since excisional surgery is increasing in popularity.	4
44. Munro NP, Woodhams S, Nawrocki JD, Fletcher MS, Thomas PJ. The role of transarterial embolization in the treatment of renal cell carcinoma. <i>BJU Int</i> 2003; 92(3):240-244.	4	25	Retrospective analysis of the role of transarterial renal embolization in the treatment of RCC.	Transarterial embolization is associated with minimal morbidity and complications, and subsequent symptom control is good. The effect of palliative embolization on RCC progression is unknown.	3
45. American College of Radiology. <i>Manual on Contrast Media</i> . Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/contrast_manual.aspx .	15	N/A	Guidance document on contrast media to assist radiologists in recognizing and managing risks associated with the use of contrast media.	N/A	3

Evidence Table Key

Study Type Key

Numbers 1-7 are for studies of therapies while numbers 8-15 are used to describe studies of diagnostics.

1. Randomized Controlled Trial — Treatment
2. Controlled Trial
3. Observation Study
 - a. Cohort
 - b. Cross-sectional
 - c. Case-control
4. Clinical Series
5. Case reviews
6. Anecdotes
7. Reviews

8. Randomized Controlled Trial — Diagnostic
9. Comparative Assessment
10. Clinical Assessment
11. Quantitative Review
12. Qualitative Review
13. Descriptive Study
14. Case Report
15. Other (Described in text)

Strength of Evidence Key

- Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.
- Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.
- Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.
- Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.